16TH
EDITION

Remington's

ARTHUR OSOL
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which measures the thickness in millimeters. A plus or minus 5% may be allowed, depending on the size of the tablet.

Tablet Weight

The volumetric fill of the die cavity determines the weight of the compressed tablet. In setting up the tablet machine the fill is adjusted to give the desired tablet weight. The weight of the tablet is the quantity of the granulation which contains the labeled amount of the therapeutic ingredient. After the tablet machine is in operation the weights of the tablets are checked routinely to insure that proper-weight tablets are being made. The USP has provided tolerances for the average weight of uncoated compressed tablets. Twenty tablets are weighed individually and the average weight is calculated. The variation from the average weight in the weights of not more than two of the tablets must not differ by more than the percentage listed below; no tablet differs by more than double that percentage. Tablets that are coated are exempt from these requirements but must conform to the test for content uniformity if it is applicable.

Average Weight	Percentage Difference
130 mg or less	10
More than 130 mg through 324 mg	7.5
More than 324 mg	5

Content Uniformity

In order to ensure that every tablet contains the amount of drug substance intended with little variation among tablets within a batch, the US Pharmacopeia includes the content uniformity test. Due to the increased awareness of physiological availability, the content uniformity test has been extended to monographs on all coated and uncoated tablets and all capsules intended for oral administration where the range of sizes of the dosage form available includes a 50 mg or smaller size, in which case the test is applicable to all sizes (50 mg and larger and smaller) of that tablet or capsule. The official compendia can be consulted for the details of the test. Tablet monographs with a content uniformity requirement do not have a weight variation requirement.

Tablet Disintegration

It is generally recognized that the *in vitro* tablet disintegration test does not necessarily bear a relationship to the *in vivo* action of a solid dosage form. To be absorbed, a drug substance must be in solution and the disintegration test is a measure only of the time required under a given set of conditions for a group of tablets to disintegrate into particles. In the present disintegration test the particles are those which will pass through a 10-mesh screen. In a comparison of disintegration times and dissolution rates or initial absorption rates of several brands of aspirin tablets, it was found that the faster absorbed tablets had the longer disintegration time. Regardless of the lack of significance as to *in vivo* action of the tablets, the test provides a means of control in assuring that a given tablet formula is the same as regards disintegration from one production batch to another. The disintegration test is used as a control for tablets intended to be administered by mouth, except where tablets are intended to be chewed before being swallowed or where tablets are designed to release the drug substance over a period of time.

Exact specifications are given for the test apparatus inasmuch as a change in the apparatus can cause a change in the results of the test. The apparatus consists of a basket rack holding six plastic tubes, open at the top and bottom; the bottom of the tubes is covered with 10-mesh screen. See Fig. 89-5. The basket rack is immersed in a bath of suitable liquid, held at 37°C, preferably in a 1-liter beaker. The rack moves up and down in the fluid at a specified rate. The volume of the fluid is such that on the upward stroke the wire mesh remains at least 2.5 cm below the surface of the fluid and descends to not less than 2.5 cm from the bottom on the downward stroke. Tablets are placed in each of the six cylinders along with a plastic disk over the tablet unless otherwise directed in the monograph. The plastic disks have a density which enables them to float above the tablets. The end point of the test is indicated when the tablets have passed through the screen. The plastic disks help to force any soft mass which forms through the screen.

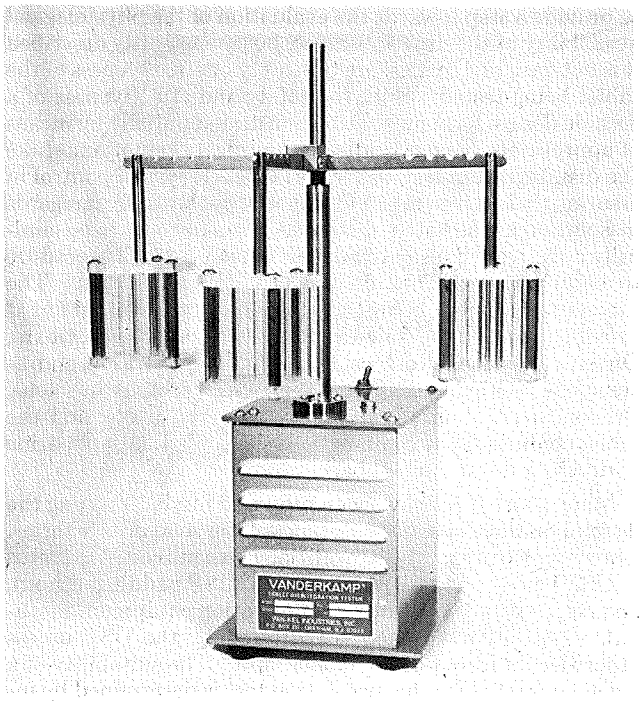


Fig. 89-5. Vanderkamp Tablet Disintegration Tester (courtesy, Van-Kel).

For compressed uncoated tablets the testing fluid is usually water at 37°C, but in some cases the monographs direct that Simulated Gastric Fluid TS be used. If one or two tablets fail to disintegrate, the test is to be repeated using 12 tablets. Of the 18 tablets then tested, 16 must have disintegrated within the given period of time. The conditions of the test are varied somewhat for coated tablets, buccal tablets, and sublingual tablets. Disintegration times are included in the individual tablet monograph. For most uncoated tablets the period is 30 min although the time for some uncoated tablets varies greatly from this. For coated tablets up to 2 hours may be required, while for sublingual tablets, such as CT Isoproterenol Hydrochloride, the disintegration time is 3 min. For the exact conditions of the test, consult the USP.

Dissolution Test

For certain tablets the monographs direct compliance with limits on dissolution rather than disintegration. Since drug absorption and physiological availability depend on having the drug substance in the dissolved state, suitable dissolution characteristics are an important property of a satisfactory tablet. Like the disintegration test, the dissolution test for measuring the amount of time required for a given percentage of the drug substance in a tablet to go into solution under a specified set of conditions is an *in vitro* test. It is intended

to provide a step towards the evaluation of the physiological availability of the drug substance, but as currently described it is not designed to measure the safety or effectiveness of the tablet being tested. Both the safety and effectiveness of a specific dosage form must be demonstrated initially by means of appropriate *in vivo* studies and clinical evaluation. Like the disintegration test, it does provide a means of control in assuring that a given tablet formulation is the same as regards dissolution as the batch of tablets shown initially to be clinically effective. It also provides an *in vitro* control procedure to eliminate variations among production batches. The tablets for which a compendial dissolution requirement is provided include the following: Acetohexamide, Digitoxin, Digoxin, Hydrochlorothiazide, Meprobamate, Methandrostenolone, Methylprednisolone, Nitrofurantoin, Prednisolone, Prednisone, Quinidine Sulfate, Sulfamethoxazole, and the tablet containing the combination of theophylline, ephedrine hydrochloride, and phenobarbital.

Many procedures have been proposed for determining the dissolution rates of active substances from solid dosage forms. Three types of apparatus are officially recognized: Apparatus 1 (USP basket method), Apparatus 2 (USP paddle method), and Apparatus 3 (modified disintegration equipment method). The basket method is preferred by the USP unless otherwise indicated in the monograph. The suitability of a given apparatus for the dissolution test is determined by individually testing one tablet of the USP Dissolution Calibrator, Disintegrating Type (a prednisone tablet), and one tablet of the USP Dissolution Calibrator, Nondisintegrating Type (a salicylic acid tablet). The given type of apparatus is suitable if the results obtained with each tablet are within the stated acceptable range for that calibrator in the apparatus tested.

Apparatus 1 consists of a 40-mesh stainless steel basket placed on the end of the stirring shaft of a variable speed motor. The basket containing the tablet or capsule is immersed in the dissolution fluid designated and rotated at a speed indicated in the monograph. The dissolution fluid specified in the monograph could be one of the following: water, buffer solution, or dilute hydrochloric acid solution. The dissolution fluid is maintained at the temperature of 37°C and the volume of the fluid kept constant by adding a volume equal to that removed for sampling purposes. Samples of the fluid are removed at designated intervals and analyzed (see Fig. 89-6).

The apparatus for the paddle method includes a round bottom, 1000-ml container which can be placed in a constant temperature bath to hold the dissolution fluid at 37°C (see Fig. 89-6). The cover for the container has three ports providing openings for the stirring shaft, thermometer, and one for the removal of samples and replacement of dissolution fluid. The stirring shaft, attached to a varying speed motor, has a blade (paddle) held in a horizontal position near the bottom of the container. The tablet is dropped into the designated fluid through one of the ports and stirred at the rate indicated in the monograph. Samples are withdrawn and analyzed at indicated intervals. Both procedures allow for manual or automated timed-sample removal and testing. The automated procedure is helpful in controlling high-volume products.

Apparatus 3 consists of a modified USP disintegration apparatus. For the dissolution application no plastic disks are used; the bottom of the basket-rack assembly descends to 1 cm from the inside bottom surface of the vessel on the downward stroke; the 10-mesh stainless steel cloth in the basket-rack assembly is replaced with 40-mesh stainless steel cloth; and the 40-mesh stainless steel cloth is fitted to the top of the basket-rack assembly to prevent the solid dosage form from floating out of the assembly's plastic tubes.

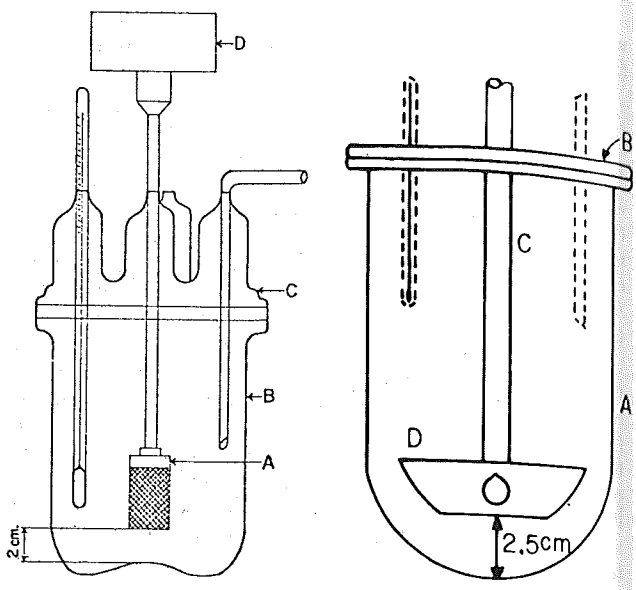


Fig. 89-6. Apparatus 1: A—rotating basket assembly; B—container for dissolution fluid; C—4-hole cover for container; D—varying speed stirring motor.

Apparatus 2: A—container for dissolution fluid; B—3-hole cover for container; C—stirring shaft attached to varying speed motor; D—stirring blade (paddle) held in horizontal position.

Details of the interpretation of dissolution test results are provided in the USP.

Methods of Preparation

Wet-Granulation Method

The most widely used and most general method of tablet preparation is the wet-granulation method. Its popularity is due to the greater probability that the granulation will meet all the physical requirements for the compression of good tablets. Its chief disadvantages are the number of separate steps involved, as well as the time and labor necessary to carry out the procedure, especially on the large scale. The steps in the wet method are (1) weighing, (2) mixing, (3) granulation, (4) screening the damp mass, (5) drying, (6) dry screening, (7) lubrication, and (8) compression. The equipment involved

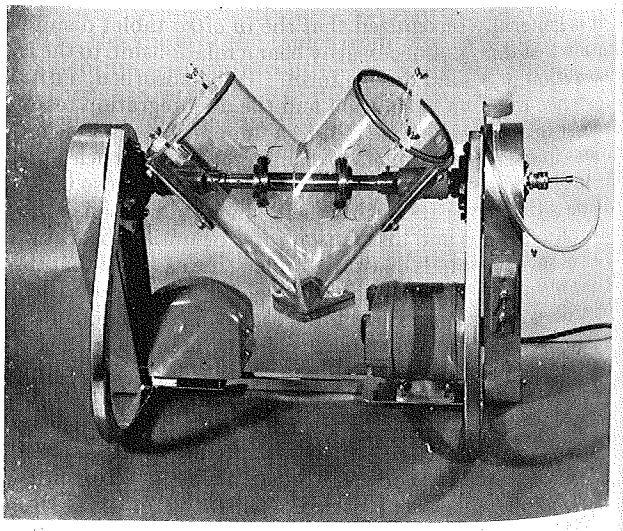
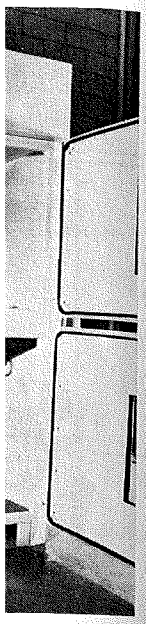


Fig. 89-7. Twin-shell blender for solids or liquid–solids blending (courtesy, Patterson-Kelley).



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After drying, the granulation is reduced in particle size by passing it through a smaller mesh screen. Following dry screening the granule size tends to be more uniform. For dry granulations the screen size to be selected depends on the diameter of the punch. The following sizes are suggested.

Tablets up to $^{3}/_{16}$-in. diam, use 20-mesh
Tablets $^{7}/_{32}$ in. to $^{5}/_{16}$ in., use 16-mesh
Tablets $^{11}/_{32}$ in. to $^{13}/_{32}$ in., use 14-mesh
Tablets $^{7}/_{16}$ in. and larger, use 12-mesh

For small amounts of granulation, hand screens may be used and the material passed through with the aid of a wooden block. With larger quantities, any of the comminuting mills with screens corresponding to those just mentioned may be used. Note that the smaller the tablet, the finer the dry granulation to enable more uniform filling of the die cavity; large granules give an irregular fill to a comparatively small die cavity. With compressed tablets of sodium bicarbonate, lactose, and magnesium trisilicate, a relationship has been demonstrated to exist between the particle size of the granulated material and the disintegration time and capping of the resultant tablets. For a sulfathiazole granulation, however, the particle-size distribution did not appear to influence hardness or disintegration.

After dry granulation, the lubricant is added as a fine powder. It is usually screened onto the granulation through 100-mesh nylon cloth to eliminate small lumps as well as to increase the covering power of the lubricant. As it is desirable for each granule to be covered with the lubricant, the lubricant is blended with the granulation very gently, preferably in a blender using tumbling action. Gentle action is desired to maintain the uniform granule size resulting from the dry-granulation step. It has been claimed that too much fine powder is not desirable because fine powder may not feed into the die evenly; consequently, variations in weight and density result. Fine powders, commonly designated as "fines," also blow out around the upper punch and down past the lower punch, making it necessary to clean the machine frequently. Air trapped in the tablets by the fine powder causes them to split apart after ejection from the machine. Fines, however, at a level of 10–20% are traditionally sought by the tablet formulator. The presence of some fines is necessary for the proper filling of the die cavity. Recently, even higher concentrations of fines were successfully used in tablet manufacture. Some investigators maintain that no general limits exist for the amount of fines that can be present in a granulation but must be determined for each specific formula.

Another approach toward the faster preparation of tablet granulations has come from the utilization of the air-suspension technique developed by Wurster.[11] In this method particles of an inert material, or the active drug, are suspended in a vertical column with a rising air stream; while the particles are suspended, the common granulating materials in solution are sprayed into the column. There is a gradual particle buildup under a controlled set of conditions resulting in a tablet granulation which is ready for compression after addition of the lubricant. In addition to its use for the preparation of tablet granulations this technique also has been proposed for the coating of solid particles as a means of improving the flow properties of small particles (see page 1587). Methods for the preparation of compressed tablets have been reviewed in the literature.[12]

In the Merck Sharp & Dohme facility at Elkton, Virginia, the entire tablet manufacturing process based on a wet-granulation method is computer-controlled. By means of a computer, the system weighs the ingredients, blends, granulates, dries, and lubricates to prepare a uniform granulation of specified particle size and particle size distribution. The computer directs the compression of the material into tablets having exacting specifications for thickness, weight, and hardness. After compression, the tablets are coated with a water-based film coating. The computer controls and monitors all flow of material. The facility represents an innovation in pharmaceutical manufacturing. See Fig. 89-14.

Dry-Granulation Method

When tablet ingredients are sensitive to moisture or are unable to withstand elevated temperatures during drying, and when the tablet ingredients have sufficient inherent binding or cohesive properties, slugging may be used to form granules. This method is referred to as dry granulation, precompression, or the double-compression method. It eliminates a number of steps but still includes (1) weighing, (2) mixing, (3) slugging, (4) dry screening, (5) lubrication, and (6) compression. The active ingredient, diluent (if one is required), and part of the lubricant are blended. One of the constituents, either the active ingredient or the diluent, must have cohesive properties. Powdered material contains a considerable amount of air; under pressure this air is expelled and a fairly dense piece is formed. The more time allowed for this air to escape, the better the tablet or slug.

When slugging is used, large tablets are made as slugs because fine powders flow better into large cavities. Also, producing large slugs decreases production time; $^{7}/_{8}$ to 1 in. are the most practical sizes for slugs. Sometimes, to obtain the pressure which is desired the slug sizes are reduced to $^{3}/_{4}$ in. The punches should be flat-faced. The compressed slugs are comminuted through the desirable mesh screen either by hand, or for larger quantities through the Fitzpatrick or similar comminuting mill. The lubricant remaining is added to the granulation, blended gently, and the material is compressed into tablets. Aspirin is a good example where slugging is satisfactory. Other materials such as aspirin combinations, acetophenetidin, thiamine hydrochloride, ascorbic acid, magnesium hydroxide, and other antacid compounds may be treated similarly.

Results comparable to those accomplished by the slugging process are also obtained with compacting mills. In the compaction method the powder to be densified passes between high-pressure rollers which compress the powder and remove the air. The densified material is reduced to a uniform granule size and compressed into tablets after the addition of a lubricant. Excessive pressures which may be required to obtain cohesion of certain materials may result in a prolonged dissolution rate. Compaction mills available include the Chilsonator (*Fitzpatrick*) and the Compactor Mill (*Allis-Chalmers*).

Direct Compression

As its name implies, direct compression consists of compressing tablets directly from powdered material without modifying the physical nature of the material itself. Formerly, direct compression as a method of tablet manufacture was reserved for a small group of crystalline chemicals having all the physical characteristics required for the formation of a good tablet. This group includes chemicals such as potassium salts (chlorate, chloride, bromide, iodide, nitrate, permanganate), ammonium chloride, and methenamine. These materials possess cohesive and flow properties which make direct compression possible.

Since the pharmaceutical industry is constantly making efforts to increase the efficiency of tableting operations and to reduce costs by utilizing the smallest amount of floor space and labor as possible for a given operation, increasing attention is being given to this method of tablet preparation. Also, this method should produce tablets of faster dissolution rates because no colloidal binders such as gelatin or starch are used to surround the granules. Approaches being used to make this method more universally applicable include the introduction of formulation additives capable of imparting the

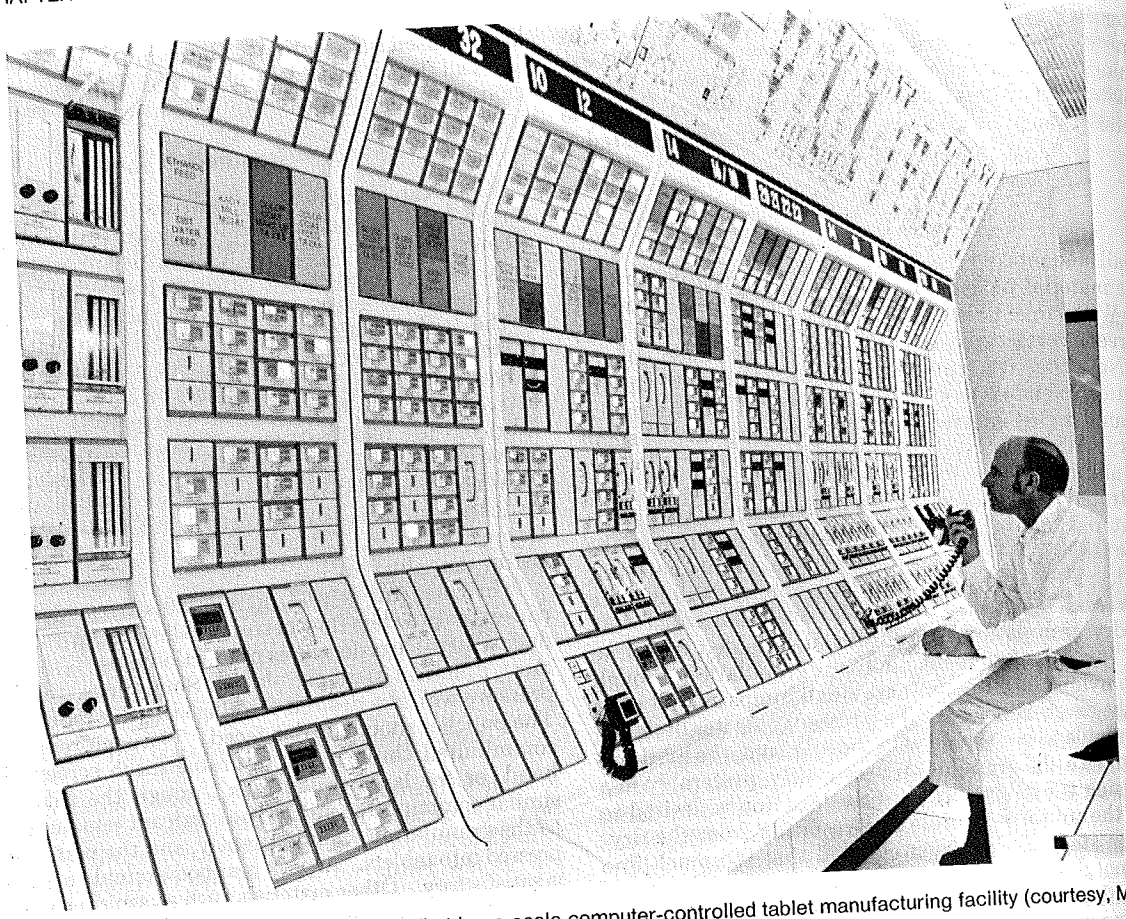

Fig. 89-14. Computer control room for the first large-scale computer-controlled tablet manufacturing facility (courtesy, MSD).

characteristics required for compression, and the use of force-feeding devices to improve the flow of powder blends.

For tablets in which the drug itself constitutes a major portion of the total tablet weight, it is necessary that the drug possess those physical characteristics required for the formulation to be compressed directly. Direct compression for tablets containing 25% or less of drug substances frequently can be used by formulating with a suitable diluent which acts as a carrier or vehicle for the drug.[13]

Direct-compression vehicles or carriers must have good flow and compressible characteristics. These properties are imparted to them by a preprocessing step such as wet granulation, slugging, spray drying, spheronization, or crystallization. These vehicles include processed forms of dicalcium phosphate dihydrate, compressible sugar, lactose, mannitol, and microcrystalline cellulose. Dicalcium phosphate dihydrate (*Di-Cal*, Stauffer) in its unmilled form has good flow properties and compressibility. It is a white crystalline agglomerate insoluble in water and alcohol. The chemical is odorless, tasteless, and nonhygroscopic. Since it has no inherent lubricating or disintegrating properties, other additives must be present to prepare a satisfactory formulation.

Compressible sugar consists mainly of sucrose that is processed to have properties suitable for direct compression. It may also contain small quantities of dextrin, starch, or invert sugar. It is a white crystalline powder with a sweet taste and complete water solubility. It requires the incorporation of a suitable lubricant at normal levels for lubricity. The sugar is widely used for chewable vitamin tablets because of its natural sweetness. One commercial source is *Di-Pac* (Amstar) prepared by the co-crystallization of 97% sucrose and 3% dextrins. Some forms of lactose meet the requirements for a direct-compression vehicle. Hydrous lactose does not flow and its use is limited to tablet formulations prepared by the wet granulation method. Both anhydrous lactose and spray-dried lactose have good flowability and compressibility and can be used in direct compression provided a suitable disintegrant and lubricant are present. Mannitol is a popular diluent for chewable tablets due to its pleasant taste and mouthfeel resulting from its negative heat of solution. In its granular form (ICI Americas) it has good flow and compressible qualities. It has a low moisture content and is not hygroscopic.

The excipient that has been studied extensively as a direct compression vehicle is microcrystalline cellulose (*Avicel*, FMC Corp.). This nonfibrous form of cellulose is obtained by spray-drying washed, acid-treated cellulose and is available in several grades which range in average particle size from 20 μm to 100 μm. It is water-insoluble but the material has the ability to draw fluid into a tablet by capillary action; it swells on contact and thus acts as a disintegrating agent. The material flows well and has a degree of self-lubricating qualities thus requiring a lower level of lubricant as compared to other excipients.

Other additives used in direct-compression formulas include cellulose [*Solka-Floc* (Brown)] and colloidal silica, such as *Cab-O-Sil* (Cabot) or *Quso* (Phila. Quartz). Silica acts as a glidant in promoting flowability of the granulation.

Forced-flow feeders are mechanical devices available from pharmaceutical equipment manufacturers designed to deaerate light and bulky material. Mechanically they maintain a steady flow of powder moving into the die cavities under moderate pressure. They attempt to minimize air entrapment and consequently capping in the finished tablet. By increasing the density of the powder, higher uniformity in tablet weights is obtained. See Fig. 89-28.

The gradual improvement of formulation additives and development of mechanical feeding devices for the high-speed

which have not been compressed, thus keeping the circular pressing compartment and the upper and lower punch guides free of dust.

Drug manufacturers have the responsibility to make certain that microorganisms present in finished products are unlikely to cause harm to the patient and will not be deleterious to the product. An outbreak of *Salmonella* infections in Scandinavian countries was traced to thyroid tablets which had been prepared from contaminated thyroid powder. This concern eventually led to the establishment of microbial limits for raw materials of animal or botanical origin, especially those that readily support microbial growth and are not rendered sterile during subsequent processing. Harmful microorganisms when present in oral products include *Salmonella* sp., *E. coli*, certain *Pseudomonas* sp. such as *Pseudomonas aeruginosa*, and *Staphylococcus aureus*. The compendia have microbial limits on raw materials such as aluminum hydroxide gel, corn starch, thyroid, acacia, and gelatin.

These represent examples of the industry's efforts to conform with the intent of current good manufacturing practice as defined by the Food and Drug Administration (see page 1436).

Tablet Formulations

Wet Granulation Method

CT Acetaminophen, 300 mg

Ingredients	In each	In 10,000
Acetaminophen	3000 mg	3000 g
Polyvinylpyrrolidone	22.5 mg	225 g
Lactose	61.75 mg	617.5 g
Alcohol 3A—200 proof	4.5 ml	45 l
Stearic acid	9 mg	90 g
Talc	13.5 mg	135 g
Corn starch	43.25 mg	432.5 g

Blend acetaminophen, polyvinylpyrrolidone, and lactose together; pass through a 40-mesh screen. Add the alcohol slowly and knead well. Screen the wet mass through a 4-mesh screen. Dry granulation at 50°C overnight. Screen the dried granulation through a 20-mesh screen. Bolt the stearic acid, talc, and corn starch through 60-mesh screen prior to mixing by tumbling with the granulation. Compress using $^{7}/_{16}$-in. standard concave punch. 10 tablets should weigh 4.5 g (courtesy, Abbott).

CT Ascorbic Acid USP, 50 mg

Ingredients	In each	In 7000
Ascorbic Acid USP (powder No. 80)[a]	55 mg	385 g
Lactose	21 mg	147 g
Starch (potato)	13 mg	91 g
Ethylcellulose N 100 (80–105 cps)	16 mg	112 g
Starch (potato)	7 mg	49 g
Talc	6.5 mg	45.5 g
Calcium stearate (impalpable powder)	1 mg	7 g
Weight of granulation		836.5 g

[a] Includes 10% in excess of claim.

Granulate the above first three ingredients with ethylcellulose (5%) dissolved in anhydrous ethyl alcohol adding additional anhydrous alcohol to obtain good wet granules. Wet screen through 8 stainless steel screen and dry at room temperature in an air-conditioned area. Dry screen through 20 stainless steel screen and incorporate the remaining three ingredients. Mix thoroughly and compress. Use a flat beveled, $^{1}/_{4}$-in. punch. 20 tablets should weigh 2.39 g.

Chewable Antacid Tablets

Ingredients	In each	In 10,000
Magnesium trisilicate	500 mg	5000 g
Aluminum hydroxide, dried gel	250 mg	2500 g
Mannitol	300 mg	3000 g
Sodium saccharin	2 mg	20 g
Starch paste, 5%	qs	qs
Oil of peppermint	1 mg	10 g
Magnesium stearate	10 mg	100 g
Corn starch	10 mg	100 g

Mix the magnesium trisilicate and aluminum hydroxide with the mannitol. Dissolve the sodium saccharin in a small quantity of purified water, then combine this with the starch paste. Granulate the powder blend with the starch paste. Dry at 140°F and screen through 16-mesh screen. Add the flavoring oil, magnesium stearate, and corn starch; mix well. Age the granulation for at least 24 hours and compress using $^{5}/_{8}$-in. flat-face bevel-edge punch (courtesy, Atlas).

CT Hexavitamin

Ingredients	In each	In 7000
Ascorbic Acid USP (powder)[a]	82.5 mg	577.5 g
Thiamine Mononitrate USP (powder)[a]	2.4 mg	16.8 g
Riboflavin[a]	3.3 mg	23.1 g
Nicotinamide USP (powder)[a]	22 mg	154 g
Starch	...	97.4 g
Lactose	...	41.2 g
Zein	...	45 g
Vitamin A acetate:	6250 U	
Vitamin D_2[a] (use Pfizer crystalets medium granules containing 500,000 U vitamin A acetate and 50,000 U vitamin D_2/g).	625 U	87.5 g
Magnesium stearate		7.5 g
Weight of granulation		1050 g

[a] Includes following excess of claim: ascorbic acid 10%, thiamine mononitrate 20%, riboflavin 10%, nicotinamide 10%, and vitamin A acetate–vitamin D_2 crystalets 25%.

Thoroughly mix the first six ingredients and granulate with zein (10% in ethyl alcohol, adding additional alcohol if necessary to obtain good wet granules). Wet screen through 8 stainless steel screen and dry at 110–120°F. Dry screen through 20 stainless steel screen and add the vitamin crystalets. Mix thoroughly, lubricate and compress. 10 tablets should weigh 1.50 g. Coat with syrup.

CT Theobromine–Phenobarbital

Ingredients	In each	In 7000
Theobromine	325 mg	2275 g
Phenobarbital	33 mg	231 g
Starch	39 mg	273 g
Talc	8 mg	56 g
Acacia (powder)	8 mg	56 g
Stearic acid	0.7 mg	4.9 g
Weight of granulation		2895.9 g

Prepare a paste with the acacia and an equal weight of starch. Use this paste for granulating the theobromine and phenobarbital. Dry and put through a 12-mesh screen, add the remainder of the material, mix thoroughly, and compress into tablets, using a $^{13}/_{32}$-in. concave punch. 10 tablets should weigh 4.13 g.

Dry Granulation Method

CT Acetylsalicylic Acid

Ingredients	In each	In 7000
Acetylsalicylic Acid (crystals 20-mesh)	0.325 g	2275 g
Starch		226.8 g
Weight of granulation		2501.8 g

Dry the starch to a moisture content of 10%. Thoroughly mix this with the acetylsalicylic acid. Compress into slugs. Grind the slugs to 14–16 mesh size. Recompress into tablets, using a $^{13}/_{32}$-in. punch. 10 tablets should weigh 3.575 g.

CT Sodium Phenobarbital

Ingredients	In each	In 7000
Phenobarbital sodium	65 mg	455 g
Milk sugar (granular, 12-mesh)	26 mg	182 g
Starch	20 mg	140 g
Talc	20 mg	140 g
Magnesium stearate	0.3 mg	2.1 g
Weight of granulation		919.1 g

Mix all the ingredients thoroughly. Compress into slugs. Grind and screen to 14–16-mesh granules. Recompress into tablets, using a $^{9}/_{32}$-in. concave punch. 10 tablets should weigh 1.3 g.

CT Vitamin B Complex

Ingredients	In each	In 10,000
Thiamine mononitrate[a]	0.733 mg	7.33 g
Riboflavin[a]	0.733 mg	7.33 g
Pyridoxine hydrochloride	0.333 mg	3.33 g
Calcium pantothenate[a]	0.4 mg	4 g
Nicotinamide	5 mg	50 g
Milk sugar (powder)	75.2 mg	752 g
Starch	21.9 mg	219 g
Talc	20 mg	200 g
Stearic acid (powder)	0.701 mg	7.01 g
Weight of granulation		1250 g

[a] Includes 10% in excess of claim.

Mix all the ingredients thoroughly. Compress into slugs. Grind and screen to 14–16-mesh granules. Recompress into tablets, using a $^{1}/_{4}$-inch concave punch. 10 tablets should weigh 1.25 g.

Sufficient tartaric acid should be used in these tablets to adjust the pH to 4.5.

Direct Compression Method

APC Tablets

Ingredients	In each	In 10,000
Aspirin (40-mesh crystal)	224 mg	2240 g
Phenacetin	160 mg	1600 g
Caffeine (Anhyd. USP gran.)	32 mg	320 g
Compressible sugar (Di-Pac[a])	93.4 mg	934 g
Sterotex	7.8 mg	78 g
Silica gel (Syloid 244[b])	2.8 mg	28 g

[a] Amstar.
[b] Davison Chem.

Blend ingredients in twin-shell blender for 15 minutes and compress on $^{13}/_{32}$-in. standard concave punch (courtesy, Amstar).

CT Ascorbic Acid USP, 250 mg

Ingredients	In each	In 10,000
Ascorbic Acid USP (Merck, fine crystals)	255 mg	2550 g
Microcrystalline cellulose[a]	159 gm	1590 g
Stearic acid	9 mg	90 g
Colloidal silica[b]	2 mg	20 g
Weight of granulation		4250 g

[a] Avicel-PH-101.
[b] Cab-O-Sil.

Blend all ingredients in a suitable blender. Compress using $^{7}/_{16}$-in. standard concave punch. 10 tablets should weigh 4.25 g (courtesy, FMC).

Breath Freshener Tablets

Ingredients	In each	In 10,000
Wintergreen oil	0.6 mg	6 g
Menthol	0.85 mg	8.5 g
Peppermint oil	0.3 mg	3 g
Silica gel (Syloid 244[a])	1 mg	10 g
Sodium saccharin	0.3 mg	3 g
Sodium bicarbonate	14 mg	140 g
Mannitol USP (granular)	180.95 mg	1809.5 g
Calcium stearate	2 mg	20 g

[a] Davison Chem.

Mix the flavor oils and menthol until liquid. Adsorb onto the silica gel. Add the remaining ingredients. Blend and compress on $^{5}/_{16}$-in. flat-face bevel-edge punch to a thickness of 3.1 mm (courtesy, Atlas).

Chewable Antacid Tablets

Ingredients	In each	In 10,000
Aluminum hydroxide and Magnesium carbonate, co-dried gel[a]	325 mg	3250 g
Mannitol USP (granular)	675 mg	6750 g
Microcrystalline cellulose[b]	75 mg	750 g
Corn starch	30 mg	300 g
Calcium stearate	22 mg	220 g
Flavor	qs	qs

[a] Reheis F-MA-11.
[b] Avicel.

Blend all ingredients in a suitable blender. Compress using $^{5}/_{8}$-in. flat-face bevel-edge punch (courtesy, Atlas).